Hybrid Phosphine/Amino-Acid Ligands Built on Phenyl and Ferrocenyl Platforms: Application in the Suzuki Coupling of *o*-Dibromobenzene with Fluorophenylboronic Acid

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We describe the synthesis and characterization of two classes of hybrid phosphino ligands functionalized with amino ester or amino acid groups. These compounds are built either on a rigid planar phenyl platform or on a functionalized – conformationally controlled – rotational ferrocene backbone. Modifications at the $-PR_2$ phosphino groups (R = aryl and alkyl, with various steric bulk, Ph, Mes, *i*-Pr, Cy) and at the amino acid/amino ester functions are reported, showing a valuable high modularity. The coordination chemistry of these compounds regarding palladium and gold was investigated, in particular with respect to the coordination mode of the phosphino groups and the preferred interaction with metals for the amino ester and amino acid functions. For all the hybrid ligands, based either on ferrocenyl or phenyl platforms, the (P,N)-chelating effect dominates in solution for coordination to Pd(II), while linear P–Au(I) complexes without interaction with the amino groups are assumed. The investigation of the catalytic activity of these new ligands in the demanding palladium-catalyzed Suzuki–Miyaura coupling of *o*-dibromoarenes with fluorophenylboronic acid underlined the importance of the amino ester dicyclohexylphosphinoferrocene for avoiding the deleterious homocoupling and arene oligomerization side-reactions that were otherwise observed with the other phosphine ligands.

Introduction

The ferrocene (Fc) platform is unique among organometallic compounds, including in the family of metallocenes, because of its stability and robustness, its versatile electroactivity, its solubility in a large diversity of solvents, and its easy derivatization towards optically pure chiral ligands.[1] Synthetic methods have been developed to build multi-functionalized ferrocenes, bearing donor (or acceptor) heteroatoms via C–H bond replacement by a great variety of C–X bonds (X = B, N, O, P, Si, Se, As, F, Cl, Br, I, *etc.*); these are often integrated into valuable chemical functions.[2]

Furthermore, the progress in transition metal chemistry is largely boosted by the development of versatile ligands (for catalysis, materials or therapeutic applications), among which phosphines is arguably the most important class.[3] Thus, the synthesis of ubiquitous phosphanyl ferrocenes has been extended to valuable hybrid compounds in which additional polar groups could be introduced. For instance, the Štěpnička group achieved the introduction of carboxyl groups,[4] various carboxamides,[5] amidosulfonates,[6] and other compounds that can serve as hybrid ligands and/or synthetic building blocks.[7] Our group has designed highly functionalized hybrid ligands and polyphosphanes (1,1′,3,3′-tetrafunctionalized) using dialkylated 1,1′-*tert*-butylferrocene as a scaffold,[8,9] These commercially available compounds promote metal-catalyzed carbon-carbon and carbon-heteroelement bond formation.[10] Analogous functionalized ferrocenes as P,B- and N,B-ambiphiles have also been synthesized, combining Lewis-acidic and Lewis-basic groups.[11,12] Such further bis-alkyl functionalization at ferrocene core introduces properties such as planar chirality and steric control over the conformation of the metallocene backbone.[10,12,13]

To the best of our knowledge, the association of amino acid functions with phosphanylferrocenes, besides their implantation on the unfunctionalized ferrocene backbone,[14] remains scarce (Scheme 1, top).[15]

Amino acids and their derivatives exhibit well-known biological activities and are widely applied as constituents of medical substances.[16] In addition, the presence of a strong electron-donating phosphino group allows, in principle, the further coordination of a transition metal, like for instance bioactive gold.[17] The recognized bio-applications of ferrocene derivatives,[18] in a first approach, make the synthesis of such amino acid hybrid ferrocenylphosphines particularly attractive, and the study of their coordination properties would open up perspectives also in the field of transition metal catalysis.[19] For

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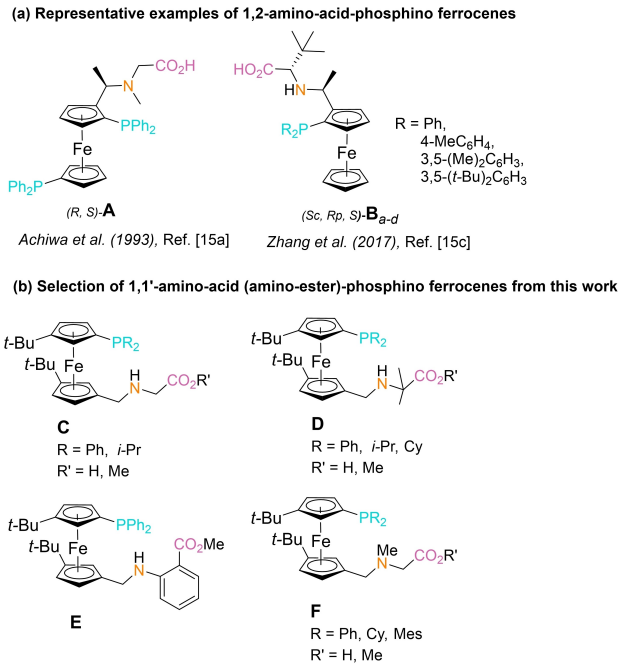


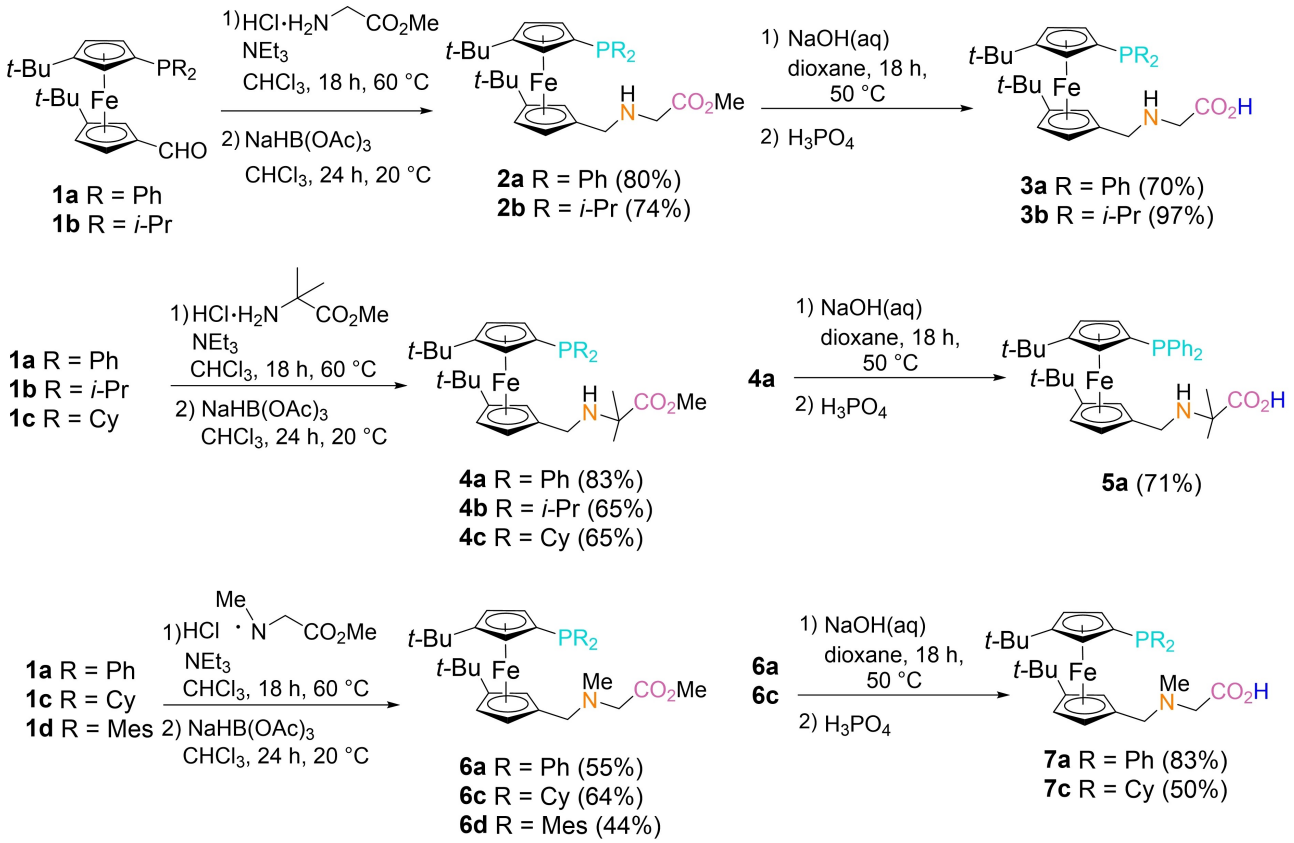
Scheme 1. Hybrid amino acid (and amino ester) phosphines built on ferrocenyl platforms.

the purpose of a coordination chemistry comparison, we in parallel achieved the synthesis of two classes of amino acid phosphines, in which the spacer between the two functions is either a large flexible rotational organometallic ferrocenyl fragment, or a smaller planar rigid phenyl functionalized at 1,2-position (Schemes 2, 3).

Results and Discussion

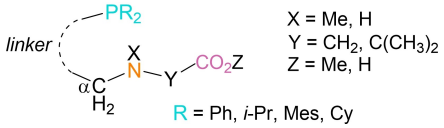
The precursors (1-phosphino-1′-carboxaldehyde-3,3′-di-*tert*-butyl)ferrocene **1a–d** (Scheme 2), synthesized from reported procedures,[11,20] were reacted with the hydrochloride esters of commercial amino acids, quantitatively obtained from reaction with $SOCl_2$ in methanol. Reductive amination of the formyl group using $NaBH(OAc)_3$ led to the formation of amino ester derivatives of glycine **2a–b** and 2-methylalanine **4a–c** in good yields ranging from 65 to 83%. This protocol could be extended to the *N*-methylated derivative of glycine (sarcosine) to form the phosphinoferrocenes **6a** and **6c–d** in 44 to 64% yield. As reported,[11b] the diastereoselective stepwise modification of di-*tert*-butylated ferrocenes with bulky alkyl groups on ferrocenes ensured planar chirality of the products formed as *rac* isomers.

The hydrolysis of **2a–b**, **4a**, **6a** and **6c** with NaOH in dioxane/water mixture, followed by acidification with H_3PO_4, proceeded cleanly to afford amino acid phosphinoferrocenes



Scheme 2. Synthesis of the *tert*-butylated phosphinoferrocene amino esters (**2a–b**, **4a–c**, **6a**, **6c–d**) and amino acids (**3a–b**, **5a**, **7a** and **7c**). The precursor compounds **1a–b** have been synthesized from reported procedures,[11b] and the synthesis of the precursor compounds **1c–d** is detailed in the Supporting Information.

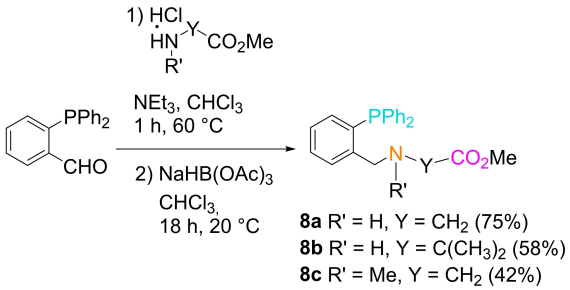
Table 1. Selected ^{31}P and ^{1}H NMR data (in $CDCl_3$) for hybrid amino acid phosphines.



	^{31}P [ppm]	αCH_2 [ppm]	CH_2 (Y) [ppm]	$C(CH_3)_2$ (Y) [ppm]	CH_3 (Z) [ppm]	CH_3 (X) [ppm]
2a	−17.2	3.08,3.30 ^{2}J 13 Hz	3.35	/	3.71	/
2b	−1.6	3.53, 3.58 ^{2}J 13 Hz	3.43	/	3.71	/
4a	−17.5	3.16, 3.27 ^{2}J 12 Hz	/	1.33, 1.37	3.70	/
4b	−1.4	3.37, 3.41 ^{2}J 12 Hz	/	1.30, 1.33	3.68	/
4c	−8.5	3.37, 3.41 ^{2}J 12 Hz	/	1.32, 1.35	3.70	/
6a	−17.3	2,96, 3.23 ^{2}J 13 Hz	3.07, 3.12 ^{2}J 16 Hz	/	3.70	2.23
6c	−8.8	3,51, 3.60 ^{2}J 13 Hz	3.16 br s	/	3.68	2.32
6d	−35.5	nd, 3.31 ^{2}J 13 Hz	3.07, 3.17 ^{2}J 16 Hz	/	3.68	2.25
8a	−15.9	3.97	3.26	/	3.60	/
8b	−15.6	3.84	/	1.23	3.64	/
8c	−14.9	3.95	3.06	/	3.66	2.16
3a[a]	−18.1	3.71,3.23 ^{2}J 13 Hz	3.27	/	/	/
3b[a]	−2.4	4.08	3.46	/	/	/
5a[a]	−18.3	3.71, 3.54 ^{2}J 13 Hz	/	1.43	/	/
7a	−17.6	3.78, 306 ^{2}J 13 Hz	3.24,3.18 ^{2}J 16 Hz	/	/	2.51
7c	−10.3	4.25, 4.09 ^{2}J 14 Hz	3.38,3.31 ^{2}J 15 Hz	/	/	2.65

[a] In MeOD for better solubility, in $CDCl_3$ otherwise.

3a–b, **5a**, **7a** and **7c**, respectively (70%, 97% 71%, 83% and 50% yield). The amino ester built on the phenyl platform, **8a–c** (Scheme 3), analogues of **2a**, **4a** and **6a**, respectively, could be synthesized following the same approach (**8a–c** in 75, 58% and 42% yield), with the synthetic advantage of an easier access to the formyl precursor 2-diphenylphosphino benzaldehyde. Table 1 summarizes some features of these various hybrid compounds, with selected data from ^{31}P and ^{1}H NMR in $CDCl_3$ solution.



Scheme 3. Straightforward synthesis of amino ester phosphinobenzenes **8a–c**. 2-Diphenylphosphino benzaldehyde from commercial source is employed.

^{31}P NMR data ranges between −1.4 ppm (P*i*-Pr_2) and −35.5 ppm ($PMes_2$) depending on the substituents at phosphorus. In the ^{1}H NMR spectra, the methylene group closer to ferrocene (αCH_2) displays two diastereotopic protons with a mutual spin coupling of ca. 13.0 Hz that contrasts with the case of the methylene located closer to carbonyl (Y) for which such distinction is not systematic nor always clear depending on the compounds.

Further characterizations were conducted in the solid state and the X-ray diffraction studies of amino esters **2a**, **6c** and **8a** could be solved (Figures 1–3). Selected distances and angles are listed in Table 2. In **2a**, the ferrocene platform adopts an eclipsed *"gauche"* conformation for the functional groups (top view, right Figure 1). The torsion angle P···Ct1···Ct2···C27 achieves a value of 65.3(1)°. The distances between the iron atom and the centroids, Fe–Ct (1.6530(18) and 1.6531(18) Å), are close to the standard value for ferrocene (1.65 Å), which shows that there is only marginal elongation of the ferrocene

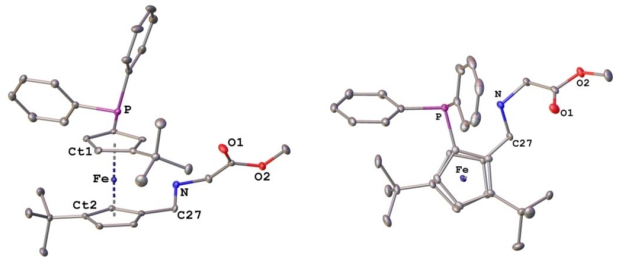


Figure 1. Views of the molecular structure of **2a**.

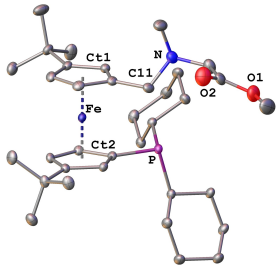


Figure 2. View of the molecular structure of **6c**.

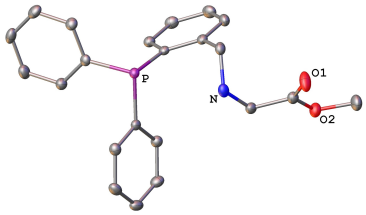


Figure 3. View of the molecular structure of **8a**.

Table 2. Selected geometric parameters for amino esters **2a**, **6c** and **8a**.

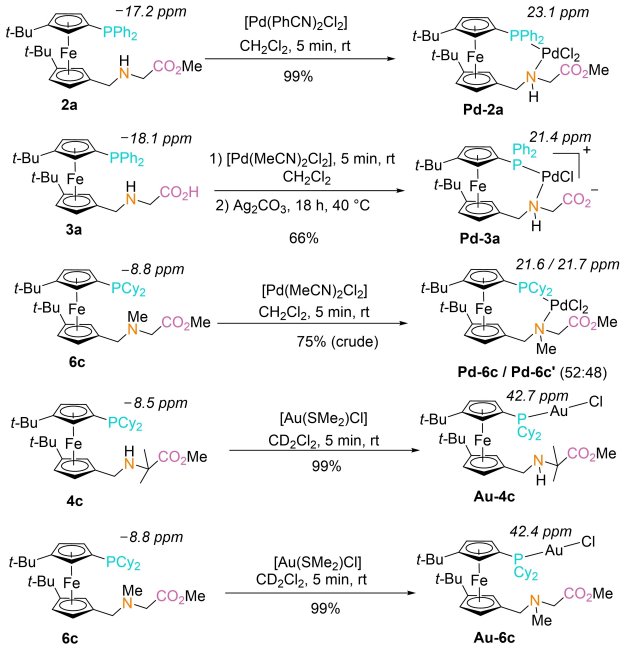
Parameter[a]	2a	6c	8a
Fe–Ct1 (Å)[a]	1.6531(18)	1.6589(9)	/
Fe–Ct2 (Å)[a]	1.6530(18)	1.6544(9)	/
P···CO_2Me (Å)	5.151(4)	5.704(2)	5.5521(16)
P···N (Å)	3.872(3)	4.5350(18)	3.1862(13)
MeO_2C···N (Å)	2.510(5)	2.532(3)	2.500(2)
Ct1–Fe–Ct2 (°)[a]	177.53(9)	178.14(5)	/
P···Ct1···Ct2···C11 (°)[a]	65.3(1)	46.48(4)	/
tilt angle (°)[b]	3.3(3)	2.54(12)	/

[a] Ct1 and Ct2 are the centroids of the phosphanyl- and ester-substituted cyclopentadienyl rings, respectively. [b] Dihedral angle of the least-squares cyclopentadienyl planes.

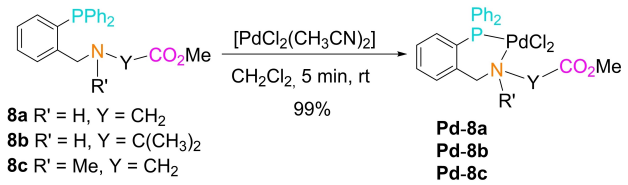
skeleton upon these multiple functionalizations. The small tilt angle and the angle Ct1–Fe–Ct2 with values of 3.3(3)° and 177.53(9)°, respectively, show a limited deformation of ferrocene. An *endo* orientation to the central iron of the amino ester functional group is established by DRX, with a direction of this group towards the phosphine substituted cyclopentadienyl plane. The distances P···N = 3.872(3) Å and P···CO_2Me = 5.151(4) Å are illustrative of the proximity between the phosphorus and nitrogen atoms, but also between phosphorus and the carbonyl fragment. The *N*-methylated amino ester **6c** shows comparable distances, with however slightly longer distances between the functional groups (P···N = 4.5350(18) Å). The XRD structure of phosphinobenzene amino ester **8a** indicates, conversely, because of the smaller rigid phenyl platform, a shorter distance P···N = 3.1862(13) Å. This collection of compounds is of interest for their multiple possibility of coordination with transition metals, as described below.

The electron-donating character of the phosphines was estimated by measuring the $^1J_{P,Se}$ coupling constants of their selenide derivatives.[13a] An increase in these coupling constants indicates an increase in the *s* character of the phosphorus lone-pair orbital, that is, an electron-withdrawing effect of the phosphane on the selenium. Compared to parent compounds **2a** and **3a**, the selenated complexes **Se(2a)** and **Se(3a)** have ^{31}P signals that were shifted to 32.0 and 31.7 ppm, with $^1J_{P=Se}$ of 729 and 731 Hz, respectively. These values indicate, compared to standard phosphinoferrocene (selenated diphenylphosphinoferrocene,[10d] $^1J_{P=Se}$ = 736 Hz) a slightly higher basicity of the phosphino group due to the introduction of the amino ester or amino acid functions.

The coordination chemistry of palladium and gold with the new hybrids was illustrated for a selection of ferrocenyl ligands **2a**, **3a**, **4c** and **6c**, and for phosphinobenzene amino esters **8a–c** (Scheme 4, Scheme 5 and Figure 4). The ^{31}P NMR spectrum of complex **Pd-2a** (Scheme 4) provides information on the coordination of phosphorus with palladium since a low field chemical shift of the phosphorus signal is observed, with a value of 23.1 ppm. Conversely to **2a**, the ^{1}H NMR analysis for **Pd-2a** shows diastereotopic protons in the form of two doublets of doublets (4.42 and 4.16 ppm) with an AB spin system separated by Δ = 0.26 ppm for the methylene CH_2 (Y, α to the ester function). The coupling constant between the two protons of CH_2 has a value $^2J_{HH}$ = 18.0 Hz, showing a strong



Scheme 4. Coordination chemistry of ferrocenyl hybrids to palladium and gold. Chemical shifts in ppm are related to ^{31}P NMR.



8a R' = H, Y = CH_2
8b R' = H, Y = $C(CH_3)_2$
8c R' = Me, Y = CH_2

Pd-8a
Pd-8b
Pd-8c

Scheme 5. Coordination chemistry of phosphinobenzene amino esters to palladium and gold.

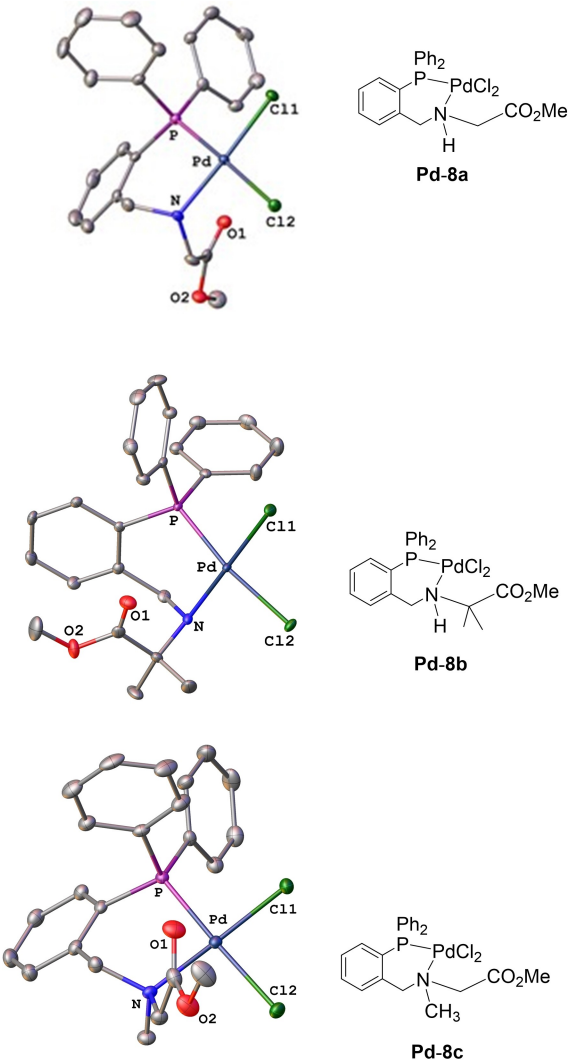


Figure 4. Pd(II) chloride coordination with chelating ligands **8a–c** (one dichloromethane molecule was omitted for clarity for **Pd-8a**, two for **Pd-8b**).

coupling constant, which indicates an interaction between palladium and nitrogen or oxygen atoms of the amino ester group at the origin of the diastereotopic methylene group. However, the methyl ester signal resonates at $\delta = 3.67$ ppm as a singlet. Because of the weak variation of the methyl resonance (δ 3.71 for **2a**), the palladium is unlikely to coordinate the oxygen in the ester and, accordingly, a P,N-chelating coordination of ligand **2a** is suggested.

The related amino acid ferrocene **3a** was also complexed with palladium. This reaction was carried out in the presence of bis[benzonitrile]Pd(II)Cl_2 in dichloromethane for five minutes at room temperature. Then, silver carbonate was added to the solution and reacted at reflux temperatures for 18 h. Silver carbonate is used to remove chlorine coordinated to palladium and deprotonates the carboxylic acid proton. Thus, **Pd-3a** is obtained with a yield of 66% and a purity of ca. 96%, due to the formation of another complex (23.2 ppm in ^{31}P NMR) in a small quantity not isolated from the main complex. ^{31}P NMR analysis yielded a signal at 21.4 ppm in MeOD (shifted from $\delta = -18.1$ for **3a**) and so confirmed the coordination of phosphorus with palladium. ^{1}H NMR spectrum of the complex shows, like for **Pd-2a**, diastereotopic methylene protons. The $CH_2CO_2^-$ group presents a signal at 3.58 ppm as a doublet ($^2J_{HH} = 15.0$ Hz) and another signal at 4.29 ppm as a doublet of doublets ($^2J_{HH} = 15.0$ Hz and $^3J_{HH} = 5.2$ Hz). The strong change of environment for these protons (for **3a**, a methylene singlet $\delta = 3.27$ ppm is observed) supports the N-coordination to Pd.

The complexation of dicyclohexylphosphinoferrocene amino ester **6c** with the precursor [Pd(MeCN)$_2$Cl$_2$] was carried out in dichloromethane at room temperature. The conversion after five minutes of reaction formed 75% of complexes **Pd-6c** and **Pd-6c′** as two diastereomers (unidentified side-products also formed). The ^{31}P NMR spectrum supports the formation of the diastereomeric complexes by the coordination of phosphorus with palladium with signals shift from going from −8.8 ppm for **6c** to 21.6 and 21.7 ppm for the palladium complex (48% and 52% from ^{1}H NMR integration). Our purification attempts failed to separate these two diastereomers. The introduction of palladium results in the formation of two diastereomers bearing a chiral center. The methyl-bearing nitrogen became a non-fluxional asymmetric center due to a strong coordination with Pd, proving the P,N-chelating coordination of ligand **3a** to the metal center.

Complexation of dicyclohexylphosphinoferrocene **6c** and **4c** was then performed with the gold(I) salt [Au(Cl)SMe$_2$] in dichloromethane at room temperature (Scheme 4). A complete conversion was obtained after 5 min, with the formation the complex **Au-6c** characterized in ^{31}P NMR by a singlet at 42.4 ppm.

A much greater chemical shift is observed for phosphorus upon coordination that is related to the linear monocoordination of gold(I) compared to P,N-chelation with **Pd-6c** and **Pd-6c′**. Accordingly, the linear coordination of gold(I) does not result in the formation of diastereomers upon complexation of gold. Unsurprisingly, a similar coordination mode was observed for the formation of **Au-4c** from **4c** with a singlet in the ^{31}P NMR spectrum at 42.7 ppm (Scheme 4). Concerning these gold complexes, the ^{1}H NMR analysis in solution confirmed that complexes and ligands are structurally close, with a net similarity of resonance for the methylene and methyl protons of the ester function (i.e., without any kind of amino ester coordination to gold). For illustration, considering **Au-4c**, the methylene protons resonate as doublets at 3.50 and 3.54 ppm ($^2J_{HH} = 12.0$ Hz), showing only a marginal variation in the chemical shift with respect to ligand **4c** (3.37 and 3.41 ppm,

Table 1). Similarly, the methyl protons of the ester function of complex **Au-4c** resonate at 3.69 ppm, while the free ligand has a signal at 3.70 ppm, also confirming the absence of coordination of gold with carbonyl oxygen.

In the ^{13}C NMR spectrum, the carbonyl carbon atom of the complex **Au-4c** resonates at 177.0 ppm, close to the chemical shift of the carbonyl carbon atom of ligand **4c** at 177.6 ppm.

The complexation of esters **8a–c** was carried out in the presence of $[PdCl_2(benzonitrile)_2]$ in dichloromethane at room temperature. The conversion is complete after five minutes. ^{31}P NMR spectra of the palladium complexes show signals at 20.2, 18.0 and 21.3 ppm for **Pd-8a–c**, respectively. The ^{1}H NMR spectra for these complexes clearly indicate that protons of the two methylene groups result in diastereotopic signals upon complexation. Thus, palladium is coordinated in a classical (P,N)-chelating motif. Any coordination of palladium with oxygen in solution is not considered, based on the marginal shift in ^{1}H NMR of the corresponding methyl ester signals, carbonyl signals in ^{13}C NMR and also IR spectroscopy. Indeed, characteristic bands for the C=O bond vibration in the Pd complexes are observed around 1726–1737 cm^{-1}, which is fully similar to the bands observed for the uncoordinated phosphinobenzenes.

XRD analysis of the complexes in the solid state confirmed this coordination mode to palladium, and typical structural values are reported in Table 3. The complexes **Pd-8a–c** form six-membered palladacycles, in a square planar geometry for a tetracoordinate palladium bound by two chlorides and the (P,N)-chelating ligands **8a–c**. The P···N distances are conserved from ligand to complexes, indicating an excellent chelating scheme for Pd.

For the complexes **Pd-8a–c**, the P–Pd–N bite angles have similar values around 93.3° and the P–Pd–Cl angles with values measured at 178.15(6)°, 168.62(2)° and 175.06(3)°, respectively, support an only slightly distorted square plane geometry. While the P···N distances are comparable to those obtained for the uncoordinated phosphinobenzene hybrid compound **8a**, the distance between the phosphine and the carbonyl of the ester group P···CO_2 = 4.069(6) Å for **Pd-8a**, 3.939(3) Å for **Pd-8b** and 4.528(3) Å for **Pd-8c** is much reduced (compared to the free ligand **8a**, P···CO_2 = 5.5521(16) Å). This geometric feature is related to the *endo* orientation of the ester fragment (in comparison to ligand **8a**), where a short distance between Pd and the oxygen atom of the carbonyl group is observed ranging between 2.994 Å and 3.152 Å. Despite repeated efforts, we did not obtain proper single crystals from the analogous phosphinoferrocene-based palladium complexes **Pd-2a**, **Pd-3a** and **Pd-6c** to compare with the XRD structures of **Pd-8a–c**, and especially identify a similar folding of the amino ester (or amino acid) toward the metal center.

Table 3. Selected geometric parameters for Pd complexes of **8a–c**.

Parameter	8a	Pd-8a	Pd-8b	Pd-8c
P···N (Å)	3.1862(13)	3.140(5)	3.1527(18)	3.172(2)
P···CO_2Me (Å)	5.5521(16)	4.069(6)	3.939(3)	4.528(3)
P–Pd–N (°)		93.23(3)	93.55(5)	93.41(6)
P–Pd–Cl2 (°)		88.16(6) / 178.15 (6)	85.67(2) / 168.62(2)	87.03(3) / 175.06(3)

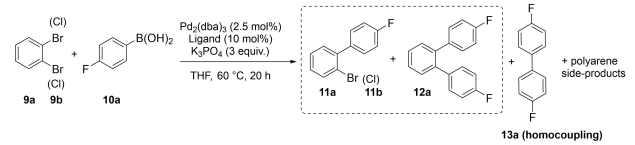
The palladium-catalyzed Suzuki-Miyaura synthesis of biphenyl motifs is a powerful method employed for synthesizing many aromatic derivatives.[21] However, the cross-coupling of polyhalogenated aromatic substrates is more challenging in terms of selectivity.[22] Notably, with electron-rich boronic acids, it may result in deleterious side-reactions, such as boronic acid homocoupling, halogenation exchange reactions or uncontrolled polyarene side-products formation. Table 4 illustrates these limitations with the palladium-catalyzed Suzuki-Miyaura coupling of *o*-dihaloarenes with fluorophenylboronic acids.

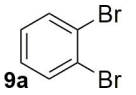
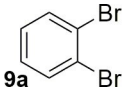
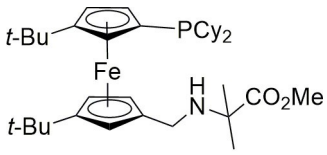
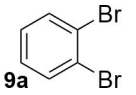
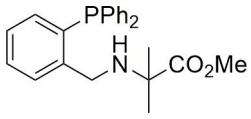
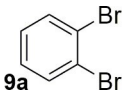
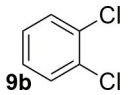
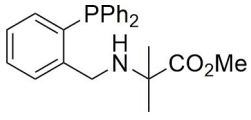
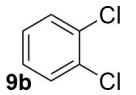
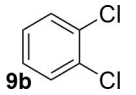
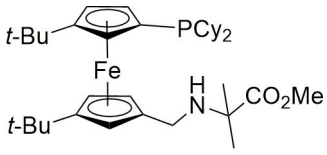
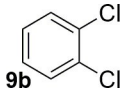
By using 2.5 mol% of $Pd_2(dba)_3$, without added ligand, in the coupling of **9a** (*o*-dibromobenzene) with **10a** (*p*-fluorophenylboronic acid) in THF at moderate temperatures (60 °C) in the presence of K_3PO_4 as base, no reaction is achieved (Table 4, entry 1). The addition of triphenylphosphine allowed the full conversion of the boronic acid with only a limited amount of monoarylated **11a** (27%) and diarylated **12a** (14%) formed (entry 2), while the major consumption of reagents is attributed to uncontrolled arene oligomerization.[23] The marginal homocoupling of fluorophenyl boronic acid to form **13a** is also detected. In screening this reaction by using the various new hybrid phosphine ligands built on phenyl and ferrocenyl platforms, we identified that the ferrocene ligand **4c** incorporating a dicyclohexyl moiety and a bulky amino ester is by far the most efficient (entry 3). In the presence of ligand **4c**, the monofunctionalized **11a** is formed in 60%, which is valuable since the bromide function would allow further functionalization. The difunctionalization is limited to 16% of **12a** with almost no homocoupling. The undesired side product formation is still present but reduced to ca. 25%. Conversely, the presence of diphenylphosphino moieties and the amino-acid-functionalized phenyl platform does not ensure the desired Suzuki coupling; this is illustrated with ligand **8b** (entry 4). These reactivity general trends were confirmed for the even more challenging arylation of dichlorobenzene **11b**, for which only using ligand **4c** allowed to produce the monochlorinated **12b** in moderate 30% yield (Table 4, entries 5–8).

Conclusions

Based on the straightforward reductive amination of carbonyl compounds, we described efficient synthetic protocols for the formation of novel hybrid compounds, which gather on a single ferrocenyl (or phenyl) platform amino ester or amino acid (derived from glycine, sarcosine, methyl-alanine) functions together with phosphino –P(aryl)$_2$ (phenyl, mesityl) or –P(alkyl)$_2$ groups (cyclohexyl, *iso*-propyl). For these *rac*-ferrocenyl compounds formed, the control of the conformation of the central platform was achieved by the use of bulky *tert*-butyl groups. These were chosen in order to favor a closer proximity of the phosphino groups with the amino ester or amino acid functions in the hybrid ligands. Multinuclear NMR spectroscopy in solution and single crystal X-ray diffraction analysis of the resulting hybrid phosphinoferrocenes and phosphinobenzenes

Table 4. Suzuki–Miyaura coupling of o-dihaloarenes with boronic acids.[a]



Entry	Ligand	Haloarene	Products
1	/	 **9a**	no reaction
2[b]	PPh_3	 **9a**	27% **11a**; 14% **12a**; 2% **13a**
3[c]	 **4c**	 **9a**	60% **11a**; 16% **12a**; traces **13a**
4	 **8b**	 **9a**	no reaction
5	/	 **9b**	no reaction
6	 **8b**	 **9b**	no reaction
7[d]	PPh_3	 **9b**	11% **13a**
8[b]	 **4c**	 **9b**	30% **11b**; 7% **12a**; traces **13a**

[a] Conditions: dihalide (0.25 mmol, 1 equiv.), aryl boronic acid (0.25 mmol, 1 equiv.), potassium phosphate (0.75 mmol, 3 equiv.), ligand (0.025 mmol, 0.1 equiv.), 3 mL THF tris(dibenzylideneacetone)dipalladium(0) (5.7 mg, 0.00625 mmol, 0.025 equiv.). [b] Full conversion of boronic acids with >55% of unidentified side-products. [c] Full conversion of boronic acid with <25% of unidentified side-products. [d] Full conversion of boronic acids with >88% of unidentified side-products. Yields determined by GC with an external standard from duplicated experiments.

were conducted, their results analyzed and compared. These compounds can be used as ligands for P,N-chelating coordination to palladium(II), and P-linear coordination to gold(I) metal centers. For ferrocenylphosphine compounds, their intrinsic Lewis basicity was estimated by $^1J_{P=Se}$ measurement after selenation. The amino ester or acid function showed little effect on the donor character of the phosphino groups. Amino acid derivatives exhibit in general biological activity, and the presence of phosphino groups allows, in addition, the coordination of bioactive metals (Au, Pt, Ru, etc.). Recognized bio-and electro-applications of ferrocene derivatives also make the present hybrids potentially attractive. Furthermore, these amino-acid and -ester ferrocenylphosphines and benzenes further open up applications as ligands for transition metal catalysis. In our contribution, the Suzuki–Miyaura arylation of *o*-dihaloarene, challenging in terms of selectivity, illustrates this potential.

Experimental Section

Materials and Methods. All reactions were performed under argon by using standard Schlenk techniques or glovebox. Hexane, pentane, THF, DMF, CH_2Cl_2, dioxane and methanol have been obtained from a solvent purification system. Chloroform was distilled from P_2O_5 under argon. The identity and purity of the products were established at the "Pôle Chimie Moléculaire" using multinuclear NMR, IR, elemental analysis and high-resolution mass spectrometry. ^{1}H NMR (500 and 600 MHz), ^{31}P NMR (202 and 243 MHz) and ^{13}C NMR (126 or 151 MHz) (including identification by 2D NMR experiments COSY, HMQC and HMBC sequences) spectra were recorded with Bruker AVANCE instrument spectrometers. Chemical shifts (δ/ppm) are given relative to internal tetramethylsilane (^{1}H and ^{13}C NMR) or to external, 85% aqueous H_3PO_4 (^{31}P NMR). FTIR spectra were recorded on a Nicolet 6700 spectrometer in the range 400–4000 cm^{-1}. Elemental analysis was performed on an Analyzer CHNS/O Thermo Electron Flash EA 1112 Series and ICP-AES iCAP Thermo. ESI mass spectra were obtained with a Bruker Compact Q-TOF spectrometer. The precursors **1a**–**b** were prepared from reported procedures.[11] Full synthetic methods and analytical data for ligands and complexes are detailed in the Supporting Information.

General procedure for the Suzuki coupling of dihalide: to a degassed mixture of aryl boronic acid (0.25 mmol, 1 equiv.), potassium phosphate (0.75 mmol, 3 equiv.), ligand (0.025 mmol, 0.1 equiv.) and 3 mL THF introduced in a tube Schlenk, were added tris(dibenzylideneacetone)dipalladium(0) (5.7 mg, 0.00625 mmol). After 10 min stirring, the dihalide (0.25 mmol, 1 equiv.) was added. The mixture was allowed to react under stirring at 60 °C for 20 h. After adding 5 mL dichloromethane to the reaction mixture, the volatiles were removed under reduced pressure. GC-MS analysis (with biphenyl external standard) was used to identify the components, and flash chromatography on silica gel (pentane : dichloromethane = 100 : 0 to 70 : 30) was used for purifying the major products.

X-Ray crystallography. Full-sphere diffraction data for **2a**, **6c**, **Pd-8a**, **Pd-8b** and **Pd-8c** were collected with a Bruker D8 VENTURE Kappa Duo PHOTON100 instrument equipped with a IμS microfocus X-ray tube. The data for other compound **8a** were recorded with a Bruker D8 Venture diffractometer. The diffractometers were equipped with Cryostream Cooler (Oxford Cryosystems) and Mo Kα radiation was used in all cases. The structures were solved by direct methods (SHELXT)[24] and then refined using a full-matrix least squares routine based on F^2 with SHELXL-2014/2018.[25] All non-hydrogen atoms were refined with anisotropic displacement parameters. Relevant crystallographic data, data collection and structure refinement parameters are presented in Supporting Information.

Deposition Numbers 2117461 (for **2a**), 2117462 (for **6c**), 2117463 (for **8a**), 2117464 (for **Pd-8a**), 2117465 (for **Pd-8b**) and 2117466 (for **Pd-8c**) contain the supplementary crystallographic data for this

paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: amino acids · amino esters · arylation ferrocenylphosphine · gold · palladium

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